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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/549,893	09/16/2005	Shigeo Yanai	68115(46590)	7166

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EXAMINER	
SASAN, ARADHANA	
ART UNIT	**PAPER NUMBER**
1615	

MAIL DATE	DELIVERY MODE
01/30/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/549,893	YANAI ET AL.	
	Examiner	Art Unit	
	Aradhana Sasan	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 September 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/16/05 and 12/8/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application

1. Claims 1-34 are included in the prosecution.

Priority

2. Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d).

Information Disclosure Statement

3. The information disclosure statements (IDS) submitted on 9/16/05 and 12/8/05 are acknowledged. The submissions are in compliance with the provisions of 37 CFR 1.97 and 1.98. Accordingly, the examiner is considering the information disclosure statements.

See attached copy of PTO-1449.

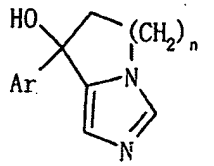
Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-6, 8, 14, 24 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Tasaka et al. (WO 02/40484).

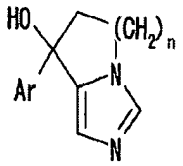
The claimed invention is a controlled release composition for oral administration which comprises a physiologically active substance which is a compound represented by the formula:



(I)-A

where n is an integer of 1 to 3, and Ar is an aromatic ring which may be substituted, or a salt thereof, and a hydrophilic polymer.

Tasaka teaches a compound of the formula:



(I)

wherein n is an integer of 1 to 3; and Ar is an optionally substituted aromatic ring, or a salt thereof (Page 4, lines 1-8). The compound (+)-6-(7-hydroxy- 6, 7-dihydro- 5H-pyrrolo [1,2-c] imidazol-7-yl)-N-methyl-2-naphthamide is disclosed as one of the compounds (Page 6, lines 24-25). A pharmaceutical composition containing the compound, which is an antitumor agent, and which is an agent for the prophylaxis or treatment of breast cancer or prostate cancer is disclosed (Page 8, lines 6-14). Pharmaceutically acceptable carriers that are used in the composition, including an excipient, a lubricant, a binder, a disintegrating agent and a thickener are disclosed (Page 39, lines 29-33). "Preferable examples of the excipient include lactose, sucrose, D-mannitol, starch, ... Preferable examples of the lubricant include magnesium stearate, calcium stearate, talc, colloidal silica ... Preferable examples of the binder include ... hydroxypropylcellulose, hydroxypropylmethylcellulose ... Preferable examples of the disintegrating agent include starch, carboxymethyl cellulose,

carboxymethyl cellulose calcium, crosscarmellose sodium, sodium carboxymethyl starch ... Preferable examples of the thickener include natural gums ... Preferable examples of the solvent include ... propylene glycol ... Preferable examples of the dispersing agent include polyethylene glycol ... Preferable examples of the solubilizer include polyethylene glycol, propylene glycol ... Preferable examples of the isotonicity agent include ... glycerine ..." (Page 40, lines 4-33). The reference also discloses that a tablet, powder, granule or capsule can be prepared by adding "an excipient, a disintegrating agent, a binder, a lubricant and the like to the compound of the present invention, and subjecting the mixture to compression molding, and where necessary, coating for masking of taste, enteric coating or coating for sustention" (Page 41, lines 12-18). The pharmaceutical preparation can be administered orally (Page 42, lines 26-28) and a sustained release preparation can also be administered (Page 43, lines 8-9). Example 5 discloses the production of 6-(7-hydroxy- 6, 7-dihydro- 5H-pyrrolo [1,2-c] imidazol-7-yl)-N-methyl-2-naphthamide (Page 58, line 12 to Page 59, line 8).

Regarding instant claim 1, the controlled release composition is anticipated by the composition comprising the compound of formula (I) and the sustained release preparation disclosed by Tasaka (Page 4, lines 1-8 and Page 43, lines 8-9). The limitation of the hydrophilic polymer is anticipated by the hydroxypropylcellulose and hydroxypropylmethylcellulose taught by Tasaka (Page 40, lines 8-10).

Regarding instant claim 2, the limitation of a core that is coated with a coating layer containing a polymer is anticipated by the "enteric coating or coating for sustention" on the tablets taught by Tasaka (Page 41, lines 12-18). A coating layer will

inherently coat a core of material. An enteric coating will inherently have an enteric coating polymer or enteric coating material.

Regarding instant claims 3 and 24, the solubility of the physiologically active substance is anticipated by the compound of formula (I) disclosed by Tasaka (Page 4, lines 1-8). The solubility of a compound is an inherent property of the compound and since the compound of formula (I) is taught by Tasaka, the solubility of the compound is anticipated by Tasaka.

Regarding instant claims 4 and 6, the dissolution characteristics of the controlled release composition is anticipated by the composition comprising the compound of formula (I) and the sustained release preparation disclosed by Tasaka (Page 4, lines 1-8 and Page 43, lines 8-9). The dissolution characteristics of a composition are an inherent property of the composition and since a composition comprising the compound of formula (I) is taught by Tasaka, the dissolution characteristics of the composition is anticipated by Tasaka.

Regarding instant claim 5, the controlled release composition is anticipated by the composition comprising the compound of formula (I) disclosed by Tasaka (Page 4, lines 1-8 and Page 43, lines 8-9). The hydrophilic polymer is anticipated by the hydroxypropylcellulose and hydroxypropylmethylcellulose taught by Tasaka (Page 40, lines 8-10). The lubricant is anticipated by the magnesium stearate, calcium stearate, talc and colloidal silica taught by Tasaka (Page 40, lines 6-8).

Regarding instant claim 8, the rapid release property of the physiologically active substance in the absence of the coating layer is anticipated by the tablet without a

coating layer as disclosed in Preparation Example 2 by Tasaka (Page 76, lines 12-23). A tablet without a coating layer will inherently have the property of rapid release of the active substance when compared to a tablet with a coating layer.

Regarding instant claims 14 and 27, the use of the controlled release composition for treating prostate cancer or breast cancer is anticipated by the pharmaceutical composition used for the treatment of breast cancer or prostate cancer as taught by Tasaka (Page 8, lines 6-14). Moreover, the use of the controlled release composition for "prevention" of prostate cancer or breast cancer is an intended use and has no significance in composition claims.

Therefore, the limitations of claims are anticipated by the teachings of Tasaka.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 7, 9-12, 22-23 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tasaka et al. (WO 02/40484) in view of Okada et al. (US 5,807,880).

The teaching of Tasaka is stated above.

Tasaka does not expressly teach enteric coating agents.

Okada teaches a steroid 17-20 lyase inhibitor, a pharmaceutically acceptable salt and a pharmaceutical composition (Col. 1, lines 6-8). The solid composition for oral administration may be used in the dosage form of tablets, powders or granules. "The

tablets or pills may be coated with a gastric or enteric film such as of sucrose, gelatin, hydroxypropylcellulose, hydroxypropylmethylcellulose phthalate or the like" (Col. 10, lines 10-14).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a composition comprising the compound of formula (I) and an enteric coating, as suggested by Tasaka, combine it with the composition comprising a steroid 17-20 lyase inhibitor that may be coated with a gastric or enteric film such as hydroxypropylmethylcellulose phthalate, as suggested by Okada, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Tasaka teaches that the composition can have an enteric coating and Okada teaches the specific enteric coating agents for solid compositions of a steroid 17-20 lyase inhibitor. One with ordinary skill in the art would use enteric coatings to ensure the protection of the composition through the gastric passage and to further ensure the release of the active ingredient in the intestines.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Regarding instant claim 7, the controlled release composition is taught by the composition comprising the compound of formula (I) disclosed by Tasaka (Page 4, lines

1-8 and Page 43, lines 8-9). The hydrophilic polymer is taught by the hydroxypropylcellulose and hydroxypropylmethylcellulose by Tasaka (Page 40, lines 8-10). The lubricant is taught by the magnesium stearate, calcium stearate, talc and colloidal silica by Tasaka (Page 40, lines 6-8). The enteric coating would have been obvious over the enteric coating of the composition taught by Tasaka (Page 41, lines 12-18) in view of the hydroxypropylmethylcellulose phthalate used as an enteric coating agent, as taught by Okada (Col. 10, lines 10-14).

Regarding instant claim 9, the limitation of the core as a controlled release matrix which further comprises a hydrophilic polymer would have been obvious over the hydrophilic polymers (hydroxypropylcellulose and hydroxypropylmethylcellulose) taught by Tasaka (Page 40, lines 8-10).

Regarding instant claims 10 and 25, the limitation of the hydrophilic polymer used at about 3% to about 95% by weight would have been obvious over the hydrophilic polymers (hydroxypropylcellulose and hydroxypropylmethylcellulose) taught by Tasaka (Page 40, lines 8-10) and by the 3% of hydroxypropylcellulose (calculated 10% of 210g=21g, 21g/700g tablet core=3%) used in the tablet composition disclosed by Okada (Col. 19, lines 46-58).

Regarding instant claims 11-12, the pH dependent or delayed-dissolution type water solubility of the polymer in the coating layer and the insoluble or sparingly soluble polymer in the coating layer would have been obvious over the enteric coating of the composition taught by Tasaka (Page 41, lines 12-18) in view of the hydroxypropylmethylcellulose phthalate used as an enteric coating agent, as taught by

Okada (Col. 10, lines 10-14). One with ordinary skill in the art would know that enteric coating polymers are water insoluble, pH dependent, and delay the dissolution of the active ingredient until after the acidic pH of the gastric passage.

Regarding instant claims 22-23, the compound would have been obvious over the (+)-6-(7-hydroxy- 6, 7-dihydro- 5H-pyrrolo [1,2-c] imidazol-7-yl)-N-methyl-2-naphthamide taught by Tasaka (Page 6, lines 24-25). The disintegrant would have been obvious over the disintegrating agents taught by Tasaka (Page 40, lines 11-14). The lubricant would have been obvious over the magnesium stearate, calcium stearate, talc, colloidal silica taught by Tasaka (Page 40, lines 6-8). The enteric coating agent would have been obvious over the hydroxypropylmethylcellulose phthalate taught by Okada (Col. 10, lines 10-14). The binder would have been obvious over the lactose, sucrose, D-mannitol, starch taught by Tasaka (Page 40, lines 4-5). The plasticizer would have been obvious over the glycerin, polyethylene glycol and propylene glycol taught by Tasaka (Page 40, lines 33 and 22).

8. Claims 13, 15-21, 26 and 28-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tasaka et al. (WO 02/40484) in view of Fernandez et al. (US 3,696,188).

The teaching of Tasaka is stated above.

Tasaka does not expressly teach a coating layer which contains a physiologically active substance.

Fernandez teaches a laminated, pan-coated tablet comprising a medicament-containing or inert compressed tablet core surrounded by a plurality of pan-coated

medicament–containing subcoating layers comprised of active ingredients (Col. 3, lines 5-9).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a composition comprising the compound of formula (I) and an enteric coating, as suggested by Tasaka, combine it with the coating containing active ingredients, as suggested by Fernandez, and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Fernandez teaches that laminated tablets with a medicament in a layer surrounding the core are "useful for various purposes, such as achieving differential release in rate ..." (Col. 1, lines 14-15).

Regarding instant claim 13, the coating layer which contains a physiologically active substance would have been obvious over the coating of the composition taught by Tasaka (Page 41, lines 12-18) in view of the coating containing active ingredients, as taught by Fernandez (Col. 3, lines 5-9).

Regarding instant claims 15-20 and 26, the composition combined with at least one other controlled release composition would have been obvious over the composition comprising the compound of formula (I) as taught by Tasaka (Page 4, lines 1-8 and Page 43, lines 8-9) in view of the medicament–containing subcoating layers taught by Fernandez (Col. 3, lines 5-9). One with ordinary skill in the art would use the compound of formula (I) as the medicament in the coating layer during the process of routine experimentation in order to optimize the release profile of the active ingredient.

Regarding instant claims 21 and 34, the use of the controlled release composition for treating prostate cancer or breast cancer is taught by the pharmaceutical composition used for the treatment of breast cancer or prostate cancer as taught by Tasaka (Page 8, lines 6-14). Moreover, the use of the controlled release composition for "prevention" of prostate cancer or breast cancer is an intended use and has no significance in composition claims.

Regarding instant claims 28-33, the limitation of a different release rate of a physiologically active substance would have been obvious over the composition with the compound taught by Tasaka (Page 4, lines 1-8 and Page 43, lines 8-9) in view of the differential release rates in the coated compositions taught by Fernandez (Col. 1, lines 14-15).

Conclusion

9. No claims are allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Aradhana Sasan whose telephone number is (571) 272-9022. The examiner can normally be reached Monday to Thursday from 6:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached at 571-272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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